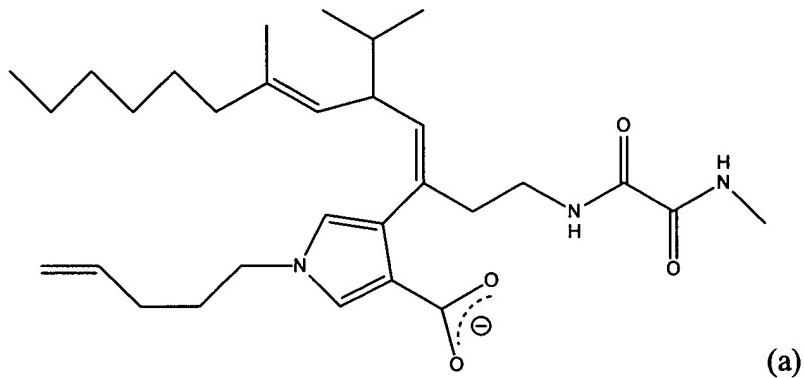
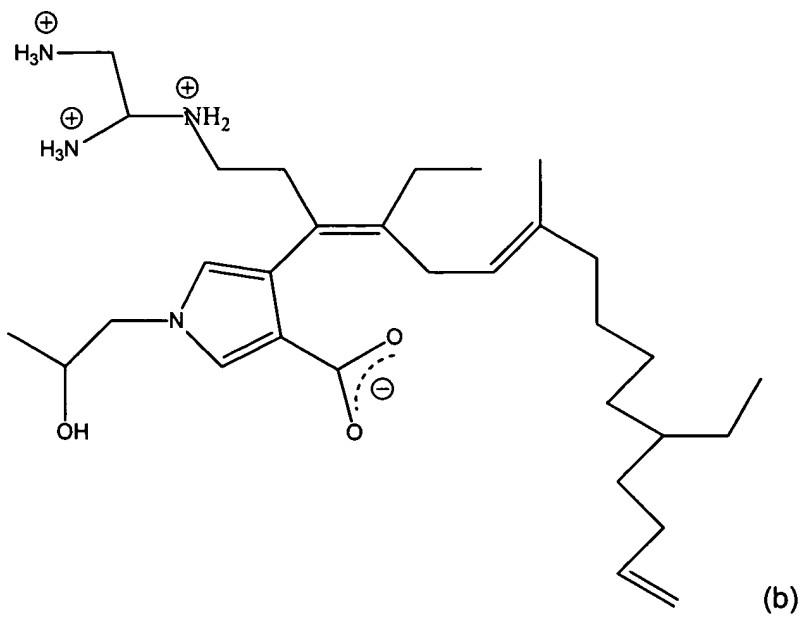


What is claimed is:

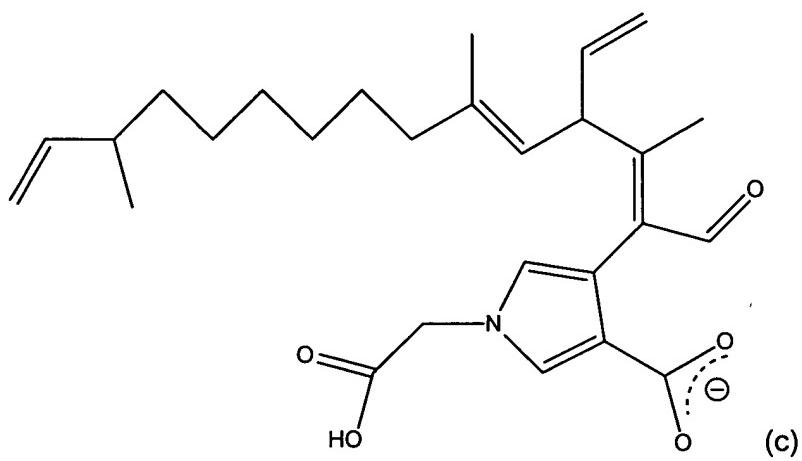
1. Use of effectors of a secondary binding site of DP IV and/or DP IV-like enzymes for the production of a medicament for the selective treatment of conditions related to DP IV enzyme activity in a mammal.
5
2. Use of effectors of a secondary binding site of DP IV and/or DP IV-like enzymes for the production of a medicament for modulating the selectivity and/or activity of DP IV or DP IV-like enzymes in a mammal.
10
3. Use of effectors of a secondary binding site of DP IV and/or DP IV-like enzymes for the production of a medicament for the prevention of the interaction of DP IV or DP IV-like enzymes with their binding proteins in a mammal.
15
4. The use according to any one of the preceding claims, wherein the secondary binding site comprises the amino acid residues L90, E91, T152, W154, W157, R310, Y330, R318, Y416, S460, K463, E464 and R560 of DP IV.
20
5. The use according to any one of claims 1, 2 or 3, wherein the secondary binding site comprises the amino acid residues Glu361 and Ile407 and Nε2 of His363 of DP IV.
25
6. The use according to any one of the preceding claims, wherein the effectors block the product release site of DP IV and/or DP IV-like enzymes.
30
7. The use according to any one of the claims 1 to 5, wherein the effectors prevent the tetramerization of DP IV and/or DP IV-like enzymes.
8. The use according to any one of the preceding claims, wherein the effector comprises 3 to 20 amino acid residues.

9. The use according to any one of the preceding claims, wherein the effector comprises 5 to 12 amino acid residues.
10. The use according to any one of the preceding claims, wherein the effector comprises 5 to 7 amino acid residues.
- 5
11. The use according to any one of the preceding claims, wherein the effector is a consensus sequence of the GRF-peptide family, preferably TFTSDY or TFTDDY.
- 10 12. The use according to any one of the preceding claims, wherein the effector is stable in the plasma and/or serum of a mammal, preferably H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH.
- 15 13. The use according to any one of claims 1 to 7, wherein the effector is selected from the group consisting of compounds of formulas a) to d):

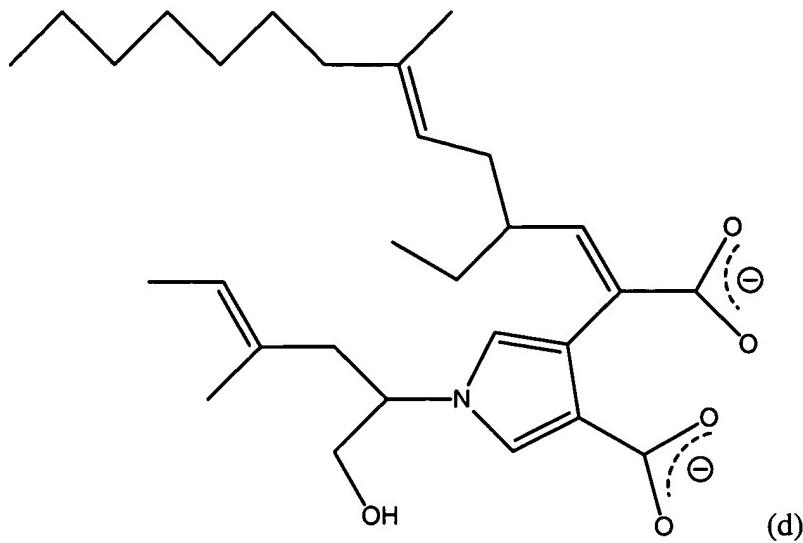




(b)



(c)



14. The use according to any one of the preceding claims, wherein the effector is
 5 administered in combination with at least one antidiabetic agent selected from the group
 consisting of

- PPAR agonists;
- biguanides, e.g. metformin, phenformin or buformin;
- protein tyrosin phosphatase-1B (PTP-1B) inhibitors;
- insulin and insulin mimetics;
- sulfonylureas and other insulin secretagogues;
- α -glucosidase inhibitors, e.g. acarbose;
- glucagon receptor agonists;
- GLP-1, GLP-1 mimetics, and GLP-1 receptor agonists;
- GLP-2, GLP-2 mimetics, and GLP-2 receptor agonists, e.g. ALX-600 (teduglutide from NPS Allelix Corp.);
- exendin-4 and exendin-4 mimetics, e.g. exenatide (AC-2993, synthetic exendin-4 from Amylin/Eli Lilly);
- GIP, GIP mimetics, and GIP receptor agonists;
- PACAP, PACAP mimetics, and PACAP receptor 3 agonists;
- PYY, PYY mimetics, PYY receptor agonists, and PYY receptor antagonists;
- cholesterol lowering agents selected from the group consisting of
 - HMG-CoA reductase inhibitors,
 - sequestrants,

- nicotinyl alkohol, nicotinic acid and salts thereof,
 - PPAR α agonists,
 - PPAR γ agonists,
 - PPAR α/γ dual agonists,
 - inhibitors of cholesterol absorption,
 - acyl CoA:cholesterol acyltransferase inhibitors, and
 - antioxidants;
- 5 - PPAR δ agonists;
- 10 - antiobesity compounds;
- 15 - an ileal bile acid transporter inhibitor; and
- 20 - anti-inflammatory agents.
15. The use according to any one of the preceding claims, wherein the effector is administered in combination with at least one DP IV-inhibitor.
16. The use according to any one of the preceding claims for the treatment of metabolic diseases, preferably Syndrome X, impaired glucose tolerance, glucosuria, lipid disorders, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL levels, high LDL levels, metabolic acidosis, hyperglycemia, diabetes mellitus, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals, metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals.
25. The use according to claims 1 to 15 for the prophylaxis and/or treatment of skin diseases, diseases of the mucosae, autoimmune diseases, inflammatory conditions, psychosomatic, neuropsychiatric and depressive illnesses, such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm and chronic pain, atherosclerosis and its sequelae, vascular restenosis, irritable bowel syndrome, inflammatory bowel disease, including Crohn's disease and ulcerative colitis, other inflammatory conditions, pancreatitis, abdominal obesity, neurodegenerative disease, retinopathy, nephropathy, ovarian hyperandrogenism (polycystic ovarian
- 30

syndrome), growth hormone deficiency, neutropenia, tumor metastasis, benign prostatic hypertrophy, gingivitis, osteoporosis, and other conditions.

18. A pharmaceutical composition comprising an effector of a secondary binding site
5 of DP IV and/or DP IV-like enzymes and a pharmaceutically acceptable carrier therefore.

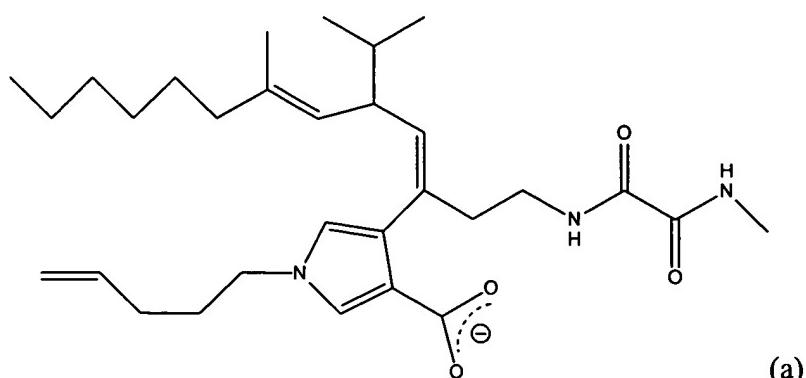
19. A pharmaceutical composition comprising an effector of a secondary binding site
of DP IV and/or DP IV-like enzymes, an antidiabetic agent and a pharmaceutically
acceptable carrier therefore.

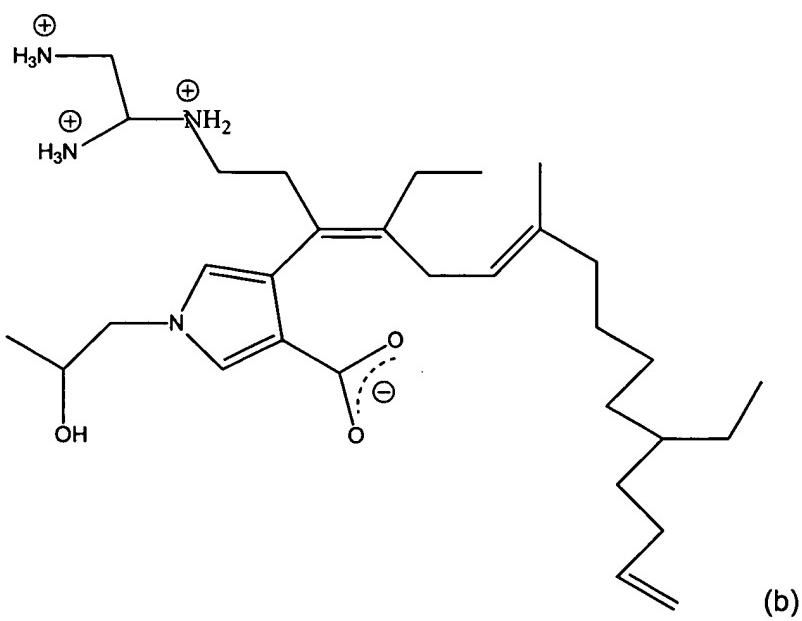
- 10 20. A pharmaceutical composition comprising an effector of a secondary binding site
of DP IV and/or DP IV-like enzymes, a DP IV-inhibitor and a pharmaceutically
acceptable carrier therefore.

- 15 21. An effector of a secondary binding site of DP IV and/or DP IV-like enzymes of
the formula TFTSDY or TFTDDY.

22. An effector of a secondary binding site of DP IV and/or DP IV-like enzymes of
the formula H-Ser-D-Glu-Thr-Gly-D-Val-D-Lys-D-Val-OH.

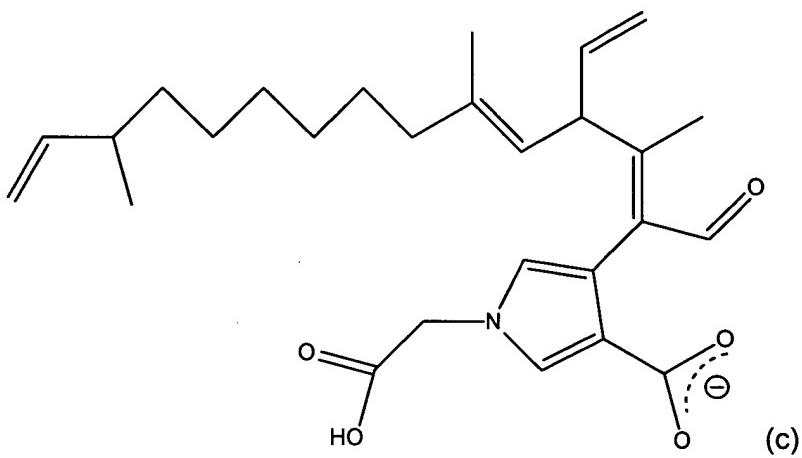
- 20 23. An effector of a secondary binding site of DP IV and/or DP IV-like enzymes
selected from the group consisting of compounds of formulas a) to d):



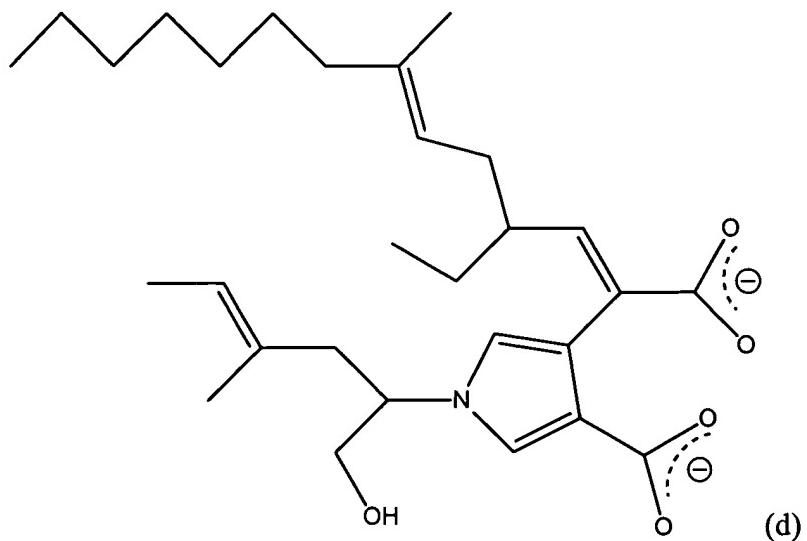


(b)

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(c)



24. A method for screening effectors capable of binding to a secondary binding site of DP IV and/or DP IV-like enzymes comprising the following steps:

- 5 a) Contacting at least one of that effectors with DP IV and/or a DP IV-like enzyme, preferably under conditions which permit binding there between;
- b) Adding a substrate of DP IV and/or DP IV-like enzymes to said DP IV and/or DP IV-like enzyme;
- c) Monitoring the biodegradation of the substrate and/or measuring the residual DP IV and/or DP IV-like enzyme activity;
- d) Correlating changes in the biodegradation and/or enzyme activity with the binding of said effectors to DP IV and/or DP IV-like enzymes; and
- e) Identification of selectivity and/or activity modifying effectors.

15 25. A method for detecting the presence of secondary binding site(s) of DP IV and/or DP IV-like enzymes comprising the following steps:

- 20 a) Providing two or more different substrates, each having an amino acid sequence, which binds to DP IV and/or DP IV-like enzymes and aligning the amino acid sequences of said substrates;
- b) Identifying at least one consensus sequence amongst said substrate amino acid sequences;
- c) Synthesizing a peptide having said consensus sequence;

5

- d) Contacting said synthesized peptide with DP IV and/or a DP IV-like enzyme;
- e) Adding a substrate of DP IV and/or a DP IV-like enzyme to the DP IV and/or DP IV-like enzyme;
- f) Monitoring the biodegradation of the substrate and/or measuring the residual DP IV and/or DP IV-like enzyme activity; and
- g) Correlating changes in said biodegradation and/or enzyme activity with the presence of a secondary binding site capable of modulating the substrate specificity of DP IV and/or DP IV-like enzymes.

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